EXHIBIT G

The efficacy of Marlex mesh in the repair of severe, recurrent vaginal prolapse of the anterior midvaginal wall

Thomas M. Julian, MD

Madison, Wisconsin

OBJECTIVE: The study assesses the efficacy and complications of Marlex mesh in repairing severe recurrent anterior vaginal wall prolapse.

STUDY DESIGN: Twenty-four patients with two or more postsurgical recurrences of severe anterior vaginal wall prolapse were divided into control and treatment groups. Transvaginal repair was similar between groups except for reinforcement of the anterior vaginal wall with synthetic mesh. Two examiners graded preoperative and postoperative support over the following 2 years ($K = 0.9$). Fisher's exact test, log-linear analysis, and analysis of variance were used to compare categoric and continuous variables.

RESULTS: Four patients in the control group and none in the treatment group had recurrent anterior vaginal wall prolapse ($p < 0.05$). Three patients had mesh-related complications.

CONCLUSION: Repair with a synthetic mesh decreased the expected incidence of severe recurrent anterior vaginal prolapse but was associated with common complications related to synthetic mesh. Mesh reinforcement is an effective treatment for severe recurrent prolapse of the anterior midvaginal wall. (Am J Obstet Gynecol 1996;175:1472-5.)

Key words: Pelvic support defects, anterior vaginal repair, recurrent vaginal prolapse

In the practice of vaginal reparative surgery, the most common site for recurrent pelvic support defects is the anterior vaginal segment, with failure rates reported from approximately 20% to 40%.[1-3] This was true and unacceptable in my own practice, especially in patients referred with previous attempts at repair. Attempting to lower my own failure rate, I changed to permanent suture for repair and extended the procedure from traditional anterior and posterior colporrhaphy to include needle urethropexy, bilateral transvaginal paravaginal defect repair, sacrospinous ligament fixation or prespinous repair, and enterocele repair or prophylaxis. This decreased the anterior vaginal wall recurrence rate from about 30% to 20%, but failures were still common, most often in the anterior vaginal segment. Patients returned with well-supported vaginal fornices and a central recurrence in the anterior vaginal segment. I was concerned that the underlying connective tissue of the anterior vaginal wall was too weak to provide adequate support. To treat this problem, a Marlex polypropylene mesh (Bard Vascular System Division, CR Bard, Billerica, Mass.) was placed in the trapezoidal area under the anterior vaginal wall segment created after anterior colporrhaphy, paravaginal repair, and urethral suspension.

Material and methods

Prospectively from January 1989 to December 1992, 24 patients were divided into control (12 patients) or treatment (12 patient) groups. All patients had at least two previous reparative procedures on the anterior vaginal wall (control group mean 2.3, range 2 to 4; treatment group 2.4, range 2 to 4) and at surgery had third- or fourth-degree support defects of the anterior vaginal segment. All patients desired preservation of vaginal function.

The control group was further divided into two groups, consisting of the first six patients assigned to the study and the last six patients, to control for unrecognized changes in technique or changing operator experience over time. Support defects were repaired similarly in each group except that the anterior vaginal segment was reinforced in the treatment group by sewing the synthetic nonabsorbable mesh from the urethrovesicle junction anteriorly to the vaginal apex posteriorly and to the junction of the obturator and levator fascia at the lateral margins of this space (Fig. 1). This mesh was placed in the treatment group after Pereyra urethropexy, anterior colporrhaphy, and bilateral transvaginal and paravaginal defect repair (Fig. 2) to restore the anterior vaginal segment. Additional procedures performed (not on the anterior vaginal wall) on all patients included sacrospinous ligament fixation or prespinous vaginal fixation, enterocele repair, and rectocele repair.

Patients were examined by the author and a second examiner (not the same examiner for all cases) preoperatively and postoperatively at approximately 6 weeks, 6

Fig. 1. Trapezoidal space formed after urethropexy, anterior colporrhaphy, and bilateral paravaginal defect is reinforced with polypropylene mesh by anchoring it at urethrovesicle junction *(u)*, posteriorly into vaginal apex *(a)*, and laterally to levator-obturator junction *(j)*.

Fig. 2. One side of completed paravaginal defect repair. Sutures join levator and obturator fascia. *c*, Anteriorly shows urethral catheter; *arrows*, levator-obturator junction.

months, 1 year, and 2 years. Pelvic support defects were graded at five vaginal sites, including the urethra, anterior vaginal wall overlying the bladder, vaginal apex, posterior cul-de-sac, and posterior vaginal wall overlying the rectum. Interobserver reliability was high ($K = 0.9$). For the purposes of this study only the results for the anterior vaginal wall overlying the bladder are reported. Pelvic support of the anterior vaginal wall was graded with a system of grade 0, no defect; 1, descent to the level of the ischial spines; 2, descent to the vaginal introitus; 3, protrusion seen beyond the vaginal introitus; 4, complete eversion of the anterior vaginal wall. All patient findings were graded in the outpatient clinic with the patient in the dorsolithotomy position and performing Valsalva's maneuver.[4]

Log-linear analysis and Fisher's exact tests compared categoric variables, and analysis of variance evaluated continuous variables (STATA, Computing Resource Center, Los Angeles).

Results

There were no statistical differences between groups in patient age, parity, weight, medical complications before surgery, preoperative grades of prolapse, intraoperative blood loss, or operating time (Table I).

The number and type of concomitant reparative procedures were identical in the two groups, with the exception of the mesh placement. There were no significant intraoperative complications in any either group. None of the patients had postoperative fever or other evidence of in-hospital infection. No patient used a suprapubic catheter >10 days. No patient required more than one discharge prescription for analgesics.

Follow-up comparisons of pelvic support are made only at 2 years after surgery to simplify the analysis. There were four cases of recurrent prolapse of the anterior

vaginal segment in the control group (two grade 2, two grade 3) and none in the treatment group ($p < 0.05$).

There were three long-term graft complications, all noted within 6 months of surgery. The most significant graft-related complication was a 0.5 cm opening below the graft that caused abnormal discharge (Fig. 3). Given the option of partial graft removal, the patient requested primary closure against medical advice. This procedure failed, leaving a slightly larger opening. The patient was again offered removal of part of the graft but did not want to risk prolapse.

The second graft complication was a 3 mm area of granulation tissue over the graft, causing spotting in an 80-year-old woman. Silver nitrate cautery failed to resolve the granulation tissue. When assured that bleeding did not indicate or increase the chance for malignancy, the patient declined further therapy.

The sexual partner of the third patient had a "lightning-like sensation on his penis" during intercourse. On inspection of the vagina for suture or a needle tip, the source could not be located. When it happened a second time, colposcopic examination showed two tiny

Table I. Demographic and operative comparisons, means and ranges

	Control	Treatment
Age (yr)	66 (46-78)	63 (37-82)
Parity	3.3 (0-11)	3.2 (0-8)
Weight (lb)	168 (108-238)	174 (132-226)
Operating time (min)	218 (186-300)	229 (191-311)
Blood loss (ml)	167 (100-300)	166 (100-300)
Preoperative to postoperative hematocrit change (%)	3.3 (2-6)	3.4 (3-6)

Fig. 3. *Arrows*, Midline vaginal defect and underlying mesh as seen through high-power colposcopic magnification.
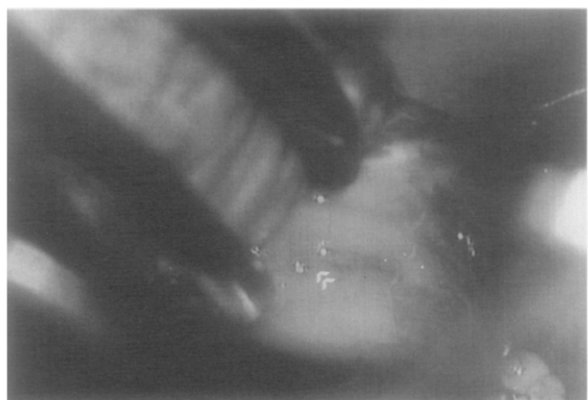
Fig. 4. *Arrows*, Two mesh strands seen as small reflections through high-power colposcopic magnification.

perforating mesh fibers. These were trimmed in the clinic, and the couple is without subsequent problems (Fig. 4).

Comment

This procedure is not recommended as a primary procedure for the repair of the anterior vaginal segment. It is reserved for patients who have had two or more reparative failures. Although not without complications, none of the complications was severe enough to make the risks greater than the benefits from this operation.

The two basic principles in pelvic reconstructive sur-

gery are simple and obvious: locate all defects and repair each defect. To accomplish this required performing reparative procedures not learned as a resident but incorporated as the need was discovered. Many reparative procedures probably fail because the operator does not or cannot identify and repair all the defects present.

The study also produced some casual observations about who is at high risk for failure after operations to correct pelvic support defects. Most obvious is that patients having two or more failed operations are at high risk. Second, the larger the degree of prolapse at the initial surgery, the greater the risk of subsequent pelvic floor defects. Third, all patients in both these groups lacked rugae on the anterior vaginal wall when they were first seen in our clinic, perhaps indicating a loss of underlying connective tissue attachment.

These patients may represent a group with systemic connective tissue weakness. This is at least anecdotally supported by the fact that 8 of these 24 patients had previous or concomitant hernia repair operations. Four had more than one such operation. This hypothesis may be partially supported by other studies suggesting that joint hypermobility may predict who is likely to have pelvic support defects after childbearing.[5]

The fear of underling connective tissue weakness is the reason that an autograft of anterior abdominal wall fascia or fascia lata from the thigh was not used in the repair rather than synthetic mesh. Now that we have a good indication of the graft efficacy, autografts or cadaver grafts may be tried.

REFERENCES

1. Morley GW, DeLancey JOL. Sacrospinous ligament fixation for eversion of the vagina. Am J Obstet Gynecol 1988;158: 872-81.
2. Shull BL, Capen CV, Riggs MW, Kuehl TJ. Preoperative and postoperative analysis of site-specific pelvic support defects in 81 women treated with sacrospinous ligament suspension and pelvic reconstruction. Am J Obstet Gynecol 1992;166: 1764-71.
3. Baden WF, Walker T. The vaginal approach to anterior vaginal defects. In: Baden WF, Walker TF, editors. Surgical repair of vaginal defects. Philadelphia: Lippincott, C 1992: 183-94.
4. Baden WF, Walker T. Evaluation of uterovaginal support. In: Baden WF, Walker TF, editors. Surgical repair of vaginal defects. Philadelphia: Lippincott, C 1992:51-62.
5. Norton PA, Baker JE, Sharp HC, Warenski JC. Genitourinary

prolapse and joint hypermobility in women. Obstet Gynecol 1995;85:225-8.

Discussion

DR. TERRY GRODY, Philadelphia, Pennsylvania. A discussion such as this is of importance to all of us because recurrent anterior pelvic compartment breakdown occurs universally with significant frequency in spite of prior objectively judged satisfactory surgical technique under the "best conditions." In this situation, such undesirable factors as avascularity, denervation, and connective tissue deficiency must be overcome. The use of mesh as described by Dr. Julian in his series of 24 patients is a prudent means by which to help solve these problems.

At Temple University we agree with the decisive number of two recurrences. We also concur that the major extra added ingredient on the next surgical venture should be customized trapezoidally shaped mesh as described. We prefer double-layered Mersilene mesh anchored with rapidly absorbable synthetic suture.

At Temple we, too, use only synthetic nonabsorbable suture for all anterior defect repairs preceding mesh application. However, we use this material not just in association with mesh and recurrences but in all operations, even the first, for anterior correction. When the worst scenario occurs, namely, hypermotile urethra, paravaginal defects, and central herniation in combination, we feel that nonabsorbable suture is critically necessary for success.

Although we also repair central distention cystocele by traditional midline imbrication and paravaginal defects by stitching to the arcus tendineus, we manage resuspension of urethrovesic junction and prolapsed urethra differently from Dr. Julian because we lack confidence in any form of needle urethropexy. Instead, as we have so long described, we use deep pubovesicocervical paracystourethral fibromuscular flaps in slinglike fashion, simultaneously also eliminating funneling, with or without simultaneous mesh placement.

When vascular deficiency is obvious or suspected, we superimpose on the mesh placement a bilateral Martius bulbocavernosus crisscross, sometimes without mesh if local tissue seems strong on tugging. The Martius bundle tips are anchored into opposite arcus tendineus fascia at the level of bladder neck.

In conclusion, (1) preoperative judgment must not be made without examination in the erect posture, not mentioned by Dr. Julian; (2) estrogen replacement, the critical catalyst to durable success, also was not mentioned; (3) as implied by Dr. Julian, restitution of normal vaginal axis by additional appropriate corrective surgery is necessary for satisfactory results; (4) slings made of transplanted autologous fascia are not to be trusted in these cases; (5) Dr. Julian has provided a significant contribution through this clinical study by use of mesh for repair.

DR. JULIAN (Closing). In response to a question, I am more adept at using the colposcope. It is easier for me.

Regarding failure at other sites, there was no statistical difference between the two groups. The reason I changed to prespinous fixation was a presentation by Dr. Meeks that interested me and led me to read an article by Inmon describing the operation in detail. It is a less deforming, better supporting operation in my hands than sacrospinous ligament fixation.

Currently I repair or prevent mesh erosion in two ways, neither of which I did in this group of patients. Under general anesthesia the patient has the area of erosion excised. A full-thickness skin graft is then placed over the mesh beneath the area of excision. The overlying vagina is closed over the skin graft.

The second technique is performed during the initial surgery. We use the vaginal flaps created during dissection of the anterior segment and close one over the other. I used to be afraid to do this because traditional wisdom suggested this would cause cyst formation. The work of Raz shows that vaginal flaps can be used without encountering this problem.

When granulation tissue occurred, it was within 6 months of the surgery and was usually present within 6 weeks. Granulation preceded erosion in the sole case of erosion in this series.

The superiority of the standing position for examination and the benefits of changing the patient to a regimen of transvaginal estrogen cream, either before or after surgery, have never been performed in a manner to clearly show that they change the outcome for patients undergoing repair of prolapse. I looked at estrogen replacement in this study, but there were too few patients to make any valid assumptions. It may be a logical assumption, but it is unproven.

The Martius graft suggested by Dr. Grody has been used in my limited experience only to fix postradiation fistulas. It is deforming and difficult to do, at least for me in the patient population I have seen. I estimate that about one third of the patients on who I have performed the Martius graft have persistent pain for months or years afterward. I would reserve it only when there are clear indications for flap grafting, rather than as prophylaxis.